1997); *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., Ltd.*, 56 U.S.P.Q.2d 1865 (Fed. Cir. 2000), *cert. granted*, 121 S. Ct. 2519 (U.S. June 18, 2001) (No. 00-1543).

Applicants respectfully request reconsideration of the pending rejections and reexamination of the present application in light of the amendments and remarks as detailed below.

Comment Regarding Claim 21

The Examiner suggests that claim 21 be revised to more clearly define the claimed subject matter. Paper No. 12 at page 2. The Applicants have amended claim 21 in accordance with the Examiner's suggestion to correct an obvious typographical error.

Rejections Under 35 U.S.C. § 112, ¶ 2

Claims 1-13 and 14-23 have been rejected under 35 U.S.C. § 112, ¶ 2, "as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." Paper No. 12 at pages 2-3. Specifically, the Examiner asserts that "defining the composition in terms of a primary sequence is vague and indefinite." *Id.* at page 2. Applicants respectfully traverse.

It is well established that a claim is valid under 35 U.S.C. § 112, ¶ 2, if one skilled in the art would understand what is claimed when the claim is read in light of the specification. *Morton Int'l Inc. v. Cardinal Chem. Co.*, 28 U.S.P.Q.2d 1190, 1194-95 (Fed. Cir. 1993); *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 1 U.S.P.Q.2d 1081, 1088 (Fed. Cir. 1986).

The attention of the Examiner is directed to the section of the instant application beginning on page 13, line 18 and ending on page 14, line 16. Applicants respectfully assert that one skilled in the art, in view of this section of the instant application, would understand the term "primary sequences" to mean, *inter alia*, amino acid sequences, the nucleic acid sequences encoding said amino acid sequences, and variants of the foregoing.

Further, claims 1-13 and 14-23 have been rejected under 35 U.S.C. § 112, ¶ 2 based on the Examiner's assertion that the term "derived" is "vague and indefinite because it only defines a starting source of material and does not describe sufficiently the end product of any number of steps involved in generating the claimed composition." Paper No. 12 at page 3. Applicants respectfully traverse.

The attention of the Examiner is directed to the section of the instant application beginning on page 13, line 24 and ending on page 14, line 16. Applicants respectfully assert that one skilled in the art, after reading this section of the instant application, would understand the meaning of the terms "derived" and "derived from" in the context of protein monomers.

Next, claims 14-16 have been rejected under 35 U.S.C. § 112, ¶ 2 based on the Examiner's assertion that clarification of the term "the primary sequences" is required. Paper No. 12 at pages 3-4. Applicants respectfully traverse.

Without acquiescing to the Examiner's rejections, and solely in order to promote the progress of the instant application, claim 14 has been amended to clarify that the term "the primary sequences" refers to the protein monomers. Applicants assert that the amendment to claim 14 obviates the Examiner's rejections.

In addition, claims 17-20 have been rejected under 35 U.S.C. § 112, ¶ 2 based on the Examiner's assertion that the recitation "said mixture" has no antecedent basis. Paper No. 12 at page 4. Applicants respectfully traverse.

The attention to the Examiner is respectfully directed to lines 6-7 of claim 17. The exposing step of claim 17 reads, "exposing said particle to a charged agent to produce *a mixture* of said monomers in a non-particle form, and." (emphasis added) The words "a mixture" in the exposing step provide proper antecedent basis for all subsequent uses of the word "mixture" within claims 17-20.

Next, claims 24-29 have been rejected under 35 U.S.C. § 112, ¶ 2 based on the Examiner's assertion that the term "associated" does not "clearly define the relation of hapten and the HBcAg." Paper No. 12 at page 4. Applicants respectfully traverse.

Without acquiescing to the rejections, and solely in order to promote the progress of the instant application, the Applicants have amended claim 24 to more clearly define the relation of duck HBcAg and a hapten within the context of the present invention by adding the terminology "linked to." As suggested by the section of the instant application beginning on page 28, line 24 and ending on page 29, line 4, the terminology "linked to" refers to either genetic linking or operative linking. Applicants assert that the amendment to claim 24 obviates the Examiner's rejections.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the present § 112 rejections.

Rejections Under 35 U.S.C. § 112, ¶ 1

Claims 2, 3, 5, 6, 8-16 and 21-29 have been rejected under 35 U.S.C. § 112, ¶ 1, based on the Examiner's contention that the inventions as claimed could not be practiced by one skilled in the art without significant and undue experimentation. Paper No. 12 at pages 4-8. Applicants respectfully traverse.

The enablement requirement of § 112 demands that the patent specification enable "those skilled in the art to make and use the full scope of the claimed invention without 'undue experimentation.'" *Genentech, Inc. v. Novo Nordisk A/S*, 42 U.S.P.Q.2d 1001, 1004 (Fed. Cir. 1997) (*quoting In re Wright*, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993)). Routine experimentation does not constitute undue experimentation. *Johns Hopkins University v. Cellpro, Inc.*, 47 U.S.P.Q.2d 1705, 1719 (Fed. Cir. 1998). Importantly, enablement is determined from the viewpoint of persons of skill in the field of the invention at the time the patent application was filed. *Ajinomoto Co. v. Archer-Daniels-Midland Co.*, 56 U.S.P.Q.2d 1332, 1337 (Fed. Cir. 2000), *cert. denied*, 121 S. Ct. 1957 (2001).

As a preliminary matter, the Applicants note that the final three paragraphs on page 5 of Paper No. 12 are incomplete. The Examiner is respectfully invited to supplement the next Office Action with the complete versions of these paragraphs if said paragraphs remain central to the Examiner's rejections under § 112.

As a second preliminary matter, the Applicants respectfully challenge the Examiner's assertion that the use of the phrase "derived from duck hepatitis B virus" provides little information regarding the biochemical structure of the "claimed monomer." Paper No. 12 at page 5. The Examiner's attention is respectfully directed to the section of the instant application beginning on page 13, line 24 and ending on page 14, line 16. Applicants respectfully assert that one skilled in the art, after reading this section of the instant application, would understand the meaning of the terms "derived" and "derived from" in the context of protein monomers.

As a third preliminary matter, the Applicants respectfully assert that the Examiner's understanding of *In re Goodman*, 29 U.S.P.Q.2d 2010 (Fed. Cir. 1993) and *In re Vaeck*, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991) outlined on page 5 of Paper No. 12 is erroneous. Neither *In re Goodman* nor *In re Vaeck* suggest that a claim drawn to a composition should be examined in light of a methodology within which said composition may be utilized.

As a fourth preliminary matter, the Applicants assert that the Examiner has rendered an improper utility rejection in the guise of a §112, ¶ 1, rejection. The attention

of the Examiner is respectfully directed to the Utility Examination Guidelines, 66 Fed. Reg. 1092 (05 January 2001).

Turning at last to the § 112, ¶ 1, rejections, the Examiner relies upon Bodey et al., 20 ANTICANCER RES. 2665-76 (2000) (hereinafter "Bodey") and Dallal & Lotze, 10(2) CANCER METASTASIS: BIOL. & CLIN. ASPECTS 433-47 (2001) (hereinafter "Dallal") in support thereof. Bodey and Dallal, according to the Examiner, allegedly suggest that extant methodologies of vaccinating against cancer yield unpredictable results and thus place "a burden upon the applicant [sic] to clearly demonstrate that an invention can function as claimed." Paper No. 12 at page 7.

The Examiner's application of the suggestions of Bodey and Dallal to the inventions claimed within the present application is manifestly inapposite. First, Bodey and Dallal fail to address the compositions and methods of vaccinating against cancer disclosed and claimed in the instant application.

Moreover, the quote from Dallal utilized by the Examiner is out of context. While Dallal does lament the rarity of unique tumor antigens, Dallal also explains that "the induction of a specific immune response is possible in a few patients through novel vaccination strategies," including strategies incorporating peptide-based vaccine therapy. Dallal at page 442. Similarly, the quote from Bodey utilized by the Examiner is out of context. While Bodey, like Dallal, laments the rarity of specific antigenic determinants on the surface of cancer cells, Bodey also explains that the immunogenicity of tumor-associated carbohydrate antigens such Globo H was "confirmed in prostate cancer patients with a broad range of stages and tumor burdens." Bodey at page 2667.

Finally, placing Bodey and Dallal aside, the Examiner has failed to recognize the success of many other groups in developing a wide variety of vaccines against cancer. Simons et al., 59 CANCER RES. 5160-68 (1999) (hereinafter "Simons"), attached as Exhibit A, reports that vaccination with irradiated GM-CSF-secreting gene-transduced cancer vaccines induces tumoricidal immune responses. Holmberg et al., 25 BONE MARROW TRANS. 1233-41 (2000) (hereinafter "Holmberg"), attached as Exhibit B, demonstrates the ability of the THERATOPE® STn-KLH cancer vaccine to decrease the risk of relapse and death in ovarian and breast cancer patients. Gong et al., 97 PNAS 2715-18 (2000) (hereinafter "Gong"), attached as Exhibit C, fusions of murine dendritic cells and murine carcinoma cells reverse unresponsiveness to tumor-associated antigens and induce the

rejection of established metastases. Hence, Examiner's contentions regarding unpredictability, in view of Bodey and Dallal, are unfounded.

Further, Applicants assert that the Examiner's contention that unpredictability "present in the art" places a burden upon any applicant to demonstrate that an invention can function as claimed runs contrary to Federal Circuit precedent. The Examiner's attention is respectfully directed to the fact that is well established that only after the USPTO provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility of a claimed invention does the burden shift to an applicant to provide rebuttal evidence to convince such a person of an invention's asserted utility. *In re Brana*, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995). Indeed, the Federal Circuit has specifically noted that usefulness in the context of 35 U.S.C. § 112, ¶ 1, and in particular in the context of pharmaceutical inventions drawn to combating cancer, necessarily "includes the expectation of further research and development." *Id.* at 1442-43.

In addition, in response to the Examiner's contention that the inventions as claimed could not be practiced by one skilled in the art without significant and undue experimentation, Applicants respectfully invite the Examiner's attention to the Declaration of Timothy P. Coleman, Ph.D., under 37 C.F.R. § 1.132, filed concurrently herewith as Exhibit D. Dr. Coleman declares that one skilled in the art, at the time of filing, would be able to make and use the inventions of the subject claims, in view of the present application, without undue experimentation. Dr. Coleman avers that this is evidenced by the results reported in the Experimental Summary attached as Exhibit 2, entitled "Analysis of the Immune Response to ΔDmuc35-DHBcAg and control antigens in BALB/c mice." Dr. Coleman asserts that that the compositions and methods successfully used in the experiments reported in Exhibit 2 were made and used by one skilled in the art in view of that which was disclosed in the present application. Dr. Coleman declares that Exhibit 2 shows that antibodies generated in mice immunized with ΔDmuc35-DHBcAg, a composition with the claims of the present application, effectively bind Muc1, a tumor-associated antigen, when Muc1 is found in its native conformation within the Muc1 positive human breast cancer cell line MCF-7.

Dr. Coleman avers that his opinion that one skilled in the art would be able to make and use the inventions of the subject claims, in view of the present application, without undue experimentation is also evidenced by the results reported in the Experimental Summary attached as Exhibit 3, entitled "Analysis of the Immune Response comparing

AAPP-MUC1 and KLH-MUC1 in BALB/c mice." Dr. Coleman asserts that the compositions and methods successfully used in the experiments reported in Exhibit 3 were made and used by one skilled in the art in view of that which was disclosed in the instant application. Dr. Coleman declares that Exhibit 3 shows that a strong immune response to AAPP-MUC1(16), a protein construct comprising the VNTR of mucin, develops in organisms injected with the protein without the use of an adjuvant, including the stimulation of IgM, IgG, IgG2a, and IgG2b antibodies.

The Examiner rejected claims 17-20 under 35 U.S.C. § 112, ¶ 1, based on the Examiner's contention that the specification "does not reasonably provide enablement" for charged agents other than Mg^{2+} or SDS. Paper No. 12 at page 8. Specifically, the Examiner contends that it is unclear that other particles would function in the same manner as Mg^{2+} without undue experimentation. *Id.* Applicants respectfully traverse.

Applicants respectfully assert that one skilled in the art can readily and routinely determine alternative charged agents without undue experimentation. Indeed, at pages 26-28, the instant application sets forth a methodology incorporating the use of charged agents other than Mg^{2+} or SDS to process particles, including but not limited to Zn^{2+}, Ba^{2+}, Ca^{2+}, Pb^{2+}, and Sr^{2+}.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the present § 112 rejections.

Rejections Under 35 U.S.C. § 102(b)

Claims 1-6, 10-13, 24-25, and 27 were rejected under 35 U.S.C. § 102(b). Paper No. 12 at page 9. Specifically, the Examiner asserts that claims 1-6, 10-13, 24-25, and 27 are anticipated by Mason et al., 36(3) J. VIROL. 829-36 (1980) (hereinafter "Mason"). *Id.* The Examiner bases the rejections on the contention that "duck HBV is associated with hepatocellular carcinoma, anticipating the requirement of haptens associated with cancer." *Id.* The Examiner also bases the rejections on the contention that "it is likely that [duck HBV] core ***antigen*** has multiple antibody binding sites, therefore, the wild type virus satisfies the limitation of containing haptens." *Id.* Applicants respectfully traverse.

Amended claim 1 is drawn to a composition comprising a plurality of recombinant nucleocapsid monomers, the primary sequences of which are derived from duck hepatitis B virus, wherein said plurality of monomers are assembled to form a particle. Independent claim 24 is drawn to a composition comprising recombinant duck HBcAg and a hapten.

In order to support an anticipation rejection under 35 U.S.C. §102, the Examiner must illustrate that each and every element of a claimed invention was disclosed within a single prior art reference. *In re Bond*, 15 U.S.P.Q.2d 1566, 1567 (Fed. Cir. 1990). In other words, the question of anticipation over a printed publication is whether a claim encompasses and would empower a patentee or assignee to exclude others from making, using, or selling a product described in said printed publication. *Helifix Ltd. v. Blok-Lok Ltd.*, 54 U.S.P.Q.2d 1299, 1304 (Fed. Cir. 2000). Critical to note is the explicit requirement that the printed publication must describe an applicant's claimed invention sufficiently to have placed a person of ordinary skill in the art in the field of the invention in possession of it. *See generally In re Paulson,* 31 U.S.P.Q.2d 1671 (Fed. Cir. 1994).

The Applicants assert that Mason, by failing to disclose each and every element of amended claim 1, did not place the composition of amended claim 1 in possession of a person of ordinary skill in the art. Specifically, Mason does not disclose the assembly of recombinant nucleocapsid monomers as defined in the composition of amended claim 1.

In addition, the Applicants assert that Mason, by failing to disclose each and every element of amended claim 24, did not place the composition of amended claim 24 in the possession of a person of ordinary skill in the art. Specifically, Mason does not disclose a hapten linked to a recombinant duck HBcAg as defined in amended claim 24.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the present § 102(b) rejections.

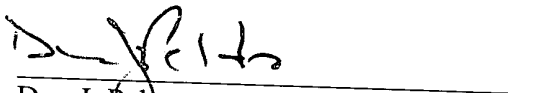
CONCLUSION

For the foregoing reasons, Applicants submit that all of the claims are in condition for allowance. Applicants respectfully request reexamination of the present application, reconsideration and withdrawal of the present rejections, and entry of the amendments. Should there be any further matter requiring consideration, the Examiner is invited to contact the undersigned counsel.

If there are any further fees due in connection with the filing of the present communication, please charge the fees to the undersigned's Deposit Account No. 50-1067. If a fee is required for an extension of time not accounted for, such an extension is requested and the fee should also be charged to the undersigned's deposit account.

Respectfully submitted,

DATE: 23 January 2002



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Claim Amendments, 23 January 2002

1. (amended) A composition [comprised of]comprising a plurality of recombinant nucleocapsid protein monomers, the primary sequences of which are derived from duck hepatitis B virus, wherein said plurality of monomers are assembled to form a particle.

2. (amended) The composition of claim 1 wherein at least a first portion of said nucleocapsid protein monomers [include]includes a first hapten.

14. (amended) A method of delivering nucleic acids to a subject in need thereof, comprising[,] administering to said subject a composition [comprised of]comprising a nucleic acid and a plurality of recombinant nucleocapsid protein monomers, wherein the primary sequences of [which]said monomers are derived from duck hepatitis B virus, wherein said plurality of monomers are assembled to form a particle, and wherein said nucleic acid is contained within said particle.

17. (amended) A nucleocapsid protein monomer particle processing method, comprising the steps of:

providing a composition [comprised of]comprising a plurality of recombinant nucleocapsid protein monomers, the primary sequences of which are derived from duck hepatitis B virus, wherein said plurality of monomers are assembled to form a particle,

exposing said particle to a charged agent to produce a mixture of said monomers in a non-particle form, and

removing said charged agent from said mixture to assemble a particle from nucleocapsid protein monomers in said mixture.

21. (amended) A method for [illiciting]eliciting an immunogenic response in a patient in need thereof, comprising the step of administering to said patient an effective amount of a composition [comprised of]comprising a plurality of recombinant nucleocapsid monomers, the primary sequences of which are derived from duck hepatitis B virus, wherein said plurality of monomers are assembled to form a particle.

24. (amended) A composition comprising

recombinant duck HBcAg; and,

a hapten, said hapten being [associated with]linked to said duck HBcAg.